

Myocardial tagging reveals a distinct regional contractility pattern after Ischemic Postconditioning in Mice

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Objective – Cardiac postconditioning (IPostC) limits reperfusion injury (1), but its effect on cardiac postischemic remodeling is insufficiently investigated. We studied cardiac morphology and global and regional contractility after IPostC in mice using cine magnetic resonance imaging (cMRI) with myocardial tagging (2) and Left Ventricular (LV) pressure conductance analysis (3).

Methods – Mice (C57BL6/J; age 12 weeks) were anesthetized with pentobarbital (50mg/kg), xylazine (2mg/kg), ketamine (30mg/kg) and atropine (0.03mg/kg). After 30min LAD occlusion in vivo, 8 mice underwent reperfusion with IPostC (3 cycles of 10 s reperfusion-reocclusion) and 9 without IPostC (noIPostC). cMRI was performed after 1 and 10 weeks using a Bruker Biospec 9.4 Tesla small animal MR scanner (Bruker BioSpin, Ettlingen, Germany; horizontal bore, 20 cm) equipped with actively shielded gradient insert (1200 mT/m) and a 3.5 cm quadrature coil (Bruker Biospin, GE). For localization purposes 2D ecg-triggered pseudo short axis and long axis T1-weighted images were recorded (FLASH, TE=1.3ms, TR=7.7ms, flip angle= 15deg, matrix 256x256, FOV 30x30mm, slice thickness= 500µm). A stack of short axis images was then recorded from base to apex (at end-systole) (12-15 frames depending on heart rate) followed by mid-level tagging imaging (SPAMM preparation and 2D FLASH cine sequence with specific parameters: TR= 9.9 ms, TE = 2.5 ms, tag spacing 400 µm, tag thickness 100 µm, field of view 30 x 30 mm, 0.6 ms block pulse of 20 deg, 10 averages using both ECG and respiration triggering). Volumes and ejection fraction (EF) were calculated using home-written software (4) and tagging grid deformation analysis with Diagnosoft 2.72 software. The papillary muscles were included in the volume analysis. Load independent preload-recrutable stroke work (PRSW) was determined using pressure conductance analysis (3). Finally, hearts were excised, weighed and collagen content determined on 5µm Sirius red-stained sections using planimetry.

Results – cMRI showed larger end-systolic and -diastolic volumes and reduced ejection fraction (EF) at both 1 and 10 weeks in noIPostC vs. others (all $p < .05$, EF at 10 weeks $45 \pm 10\%$ in noIPostC, $55 \pm 6\%$ in IPostC and $61 \pm 8\%$ in SHAM). Myocardial mass was higher in the noIPostC group vs. IPostC and sham at 10 weeks ($72 \pm 9\text{mg}$ vs. $60 \pm 13\text{mg}$ and $59 \pm 8\text{mg}$ respectively, $p < .05$). The tagging grid deformation was less in the anterolateral wall (segment 5 and 6) while the interventricular septum (segment 2) showed significantly more compensatory deformation after IPostC (fig 1), evidenced by the individual strain curves and the calculated area under the curve. PRSW was lower in the noIPostC group (51 ± 13 mmHg vs. 68 ± 7 mmHg in IPostC and 92 ± 11 mmHg in sham, both $p < .01$). The collagen content in the LV wall was higher in noIPostC (0.08 ± 0.02 vs. 0.04 ± 0.02 in IPostC and 0.02 ± 0.003 in sham, both $p < .001$, see fig 2).

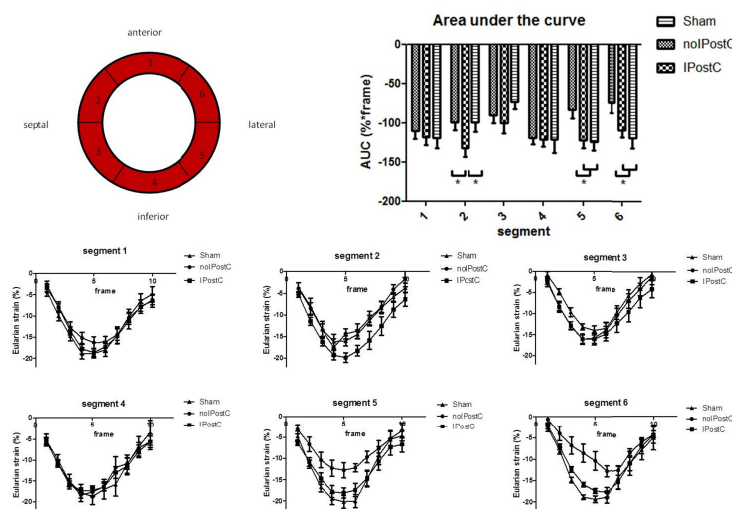


Figure 1. Segmental strain curves and calculated area under the curves (AUC) obtained by myocardial tagging after ischemia reperfusion. Mean values \pm SEM. AUC values $p < .05$ indicated with *

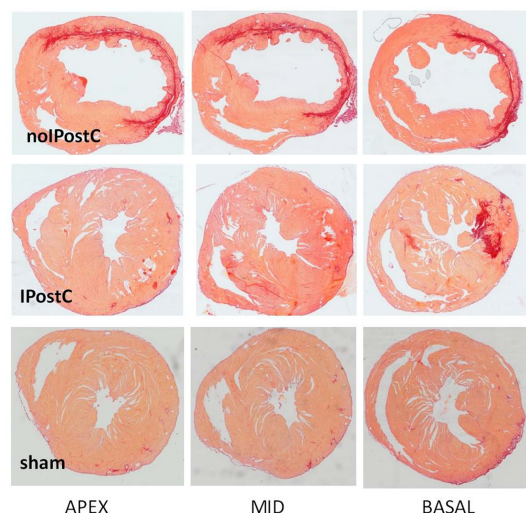


Figure 2. Sirius red staining of apical, midLV and basal slices in noIPostC, IPostC or sham group after 10 weeks follow up

Conclusions – The cardioprotective effect of IPostC, evidenced after 1 week, is sustained and protects against adverse LV remodeling. Myocardial tagging reveals an improved contractility pattern at both postischemic and remote areas, resulting in an increased global contractility.

References

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